
EXAMINER'S AMENDMENT AND REASONS FOR ALLOWANCE

Applicants' amendment and response filed 13 January 2012 to the non-final Office Action mailed 01 September 2011 is acknowledged and entered.

Also acknowledged and entered is the Declaration filed 13 January 2012 under 37 C.F.R. §1.131 from Forgacs, Jakabv, Neagu and Mironov.

Claims Status

According to the Amendment filed 13 January 2012 following is the current status of claims in the instant application:

- ⌘ Claims 85-88 have been added;
- ⌘ Claims 10, 18-51 and 67-84 remain canceled;
- ⌘ Claims 1-9 and 11-17 remain withdrawn;
- ⌘ Claims 1 and 60, have currently been amended; and
- ⌘ Claims 1-9, 11-17, 52-66 and 85-88 are currently pending and are examined on merits.

Withdrawals

All rejections in the Office Action with non-final rejection mailed 01 September 2011 are hereby withdrawn in consideration of Applicants' amendments and remarks and Declaration under 37 C.F.R. §1.131 from Forgacs, Jakabv, Neagu and Mironov filed 13 January 2012.

In accordance with Applicants' remarks and declaration cited *supra*, and the literature search for prior art and pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86), claims 1-9, 11-17 and 87-88, directed to the process of making the patentable product, previously withdrawn from consideration as a result of a restriction

requirement mailed on 09 August 2010, are now subject to being rejoined. Process claims are hereby rejoined and fully examined for patentability under 37 C.F.R. §1.104. In accordance with the Official Gazette notice, *supra*, process claims 1-9, 11-17 and 87-88 and product Claims 52-66 and 85-86 are fully examined for patentability in one single application.

Informals

The instant Non-Provisional application (i.e., 10/590,446) currently under prosecution at the United States Patent and Trademark Office (i.e., USPTO) has now **been assigned to Kailash C. Srivastava in Art Unit 1657**. To aid in correlating any papers for the instant application (i.e., 10/590,446), all further correspondence regarding the instant application (i.e., 10/590,446) should be **directed to Examiner Kailash C. Srivastava in Art Unit 1657**.

Information Disclosure Statement

The Information Disclosure Statement (i.e., IDS filed 09 February 2012 is acknowledged, made of record, considered and duly signed copy of substitute for form 1449 A/B PTO is enclosed with the instant Office Action.

Examiner's amendment

An Examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicants, an amendment may be filed as provided by 37 C.F.R. §1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this Examiner's amendment was given in a telephone interview on 22 March 2012 with Mr. J. Richards, Applicants' Representative.

In the Claims:

1. (Previously Presented) A method of producing a plurality of fused aggregates forming a desired three-dimensional structure, the method comprising: depositing a layer of a matrix on a substrate; embedding a plurality of cell aggregates, each comprising a

plurality of cells, in the layer of the matrix to form a three-dimensional layered structure of claim 52, the aggregates being arranged in a non-random predetermined pattern, wherein the cell aggregates have predetermined positions in the pattern; allowing at least one aggregate of said plurality of cell aggregates to fuse with at least one other aggregate of the plurality of cell aggregates to form the desired structure; and separating the structure from the matrix.

2. (Currently Amended) The method of claim 1, wherein the layer of the matrix constitutes a first layer, the plurality of cell aggregates constitutes a first plurality of cell aggregates, and the predetermined pattern constitutes a first predetermined pattern, the method further comprising the steps of: depositing a second layer of the matrix on the first layer; and embedding a second plurality of cell aggregates in the second layer, the second plurality of cell aggregates comprising a plurality of cells, the second plurality of cell aggregates being arranged in a second predetermined pattern, and allowing at least one cell aggregate in the first plurality of cell aggregates to fuse with at least one cell aggregate in the second plurality of cell aggregates.

3. (Currently Amended) The method of claim 2, wherein the first and second predetermined patterns are substantially the same, and wherein the second plurality of cell aggregates is embedded in the second layer of the matrix in registration with the first plurality of cell aggregates.

4. (Currently Amended) The method of claim 2, wherein the desired structure is a tube, the first and second predetermined patterns are both circular in shape, and the second plurality of cell aggregates is embedded in the second layer of the matrix in registration with the first plurality of cell aggregates.

5. (Currently Amended) The method of claim 1, wherein the thickness of the layer of the matrix is about equal to the average diameter of the plurality of cell aggregates.

6. (Currently Amended) The method of claim 1₂ wherein the cell aggregates are substantially spherical.
7. (Currently Amended) The method of claim 1₂ wherein the cell aggregates are substantially uniform in size.
8. (Currently Amended) The method of claim 1₂ wherein the cell aggregates have an average size between about 100 and about 600 microns.
9. (Currently Amended) The method of claim 8₂ wherein no more than about 10% ~~percent~~ of the cell aggregates deviate from said average size by more than 5%.
10. (Canceled)
11. (Currently Amended) The method of claim 1₂ wherein the cell aggregates consist essentially of cells of a single type.
12. (Currently Amended) The method of claim 1₂ wherein at least one of the cell aggregates comprises a plurality of living cells of a first type and a plurality of living cells of a second type that is different from the first type.
13. (Currently Amended) The method of claim 12₂ wherein said at least one cell aggregate comprises a mixture of said cells of the first type and said cells of the second type and the method further comprises the step of allowing at least some of the cells of the first type to segregate from at least some of the cells of the second type.
14. (Currently Amended) The method of claim 12₂ wherein the cells of the first type are epithelial cells and the cells of the second type are connective tissue-forming cells.
15. (Currently Amended) The method of claim 1₂ wherein the predetermined pattern comprises a ring.

16. (Currently Amended) The method of claim 1, wherein the matrix comprises a gel.

17. (Currently Amended) The method of claim 1, wherein said plurality of cell aggregates includes at least one cell aggregate consisting essentially of cells of a first type and at least one other cell aggregate consisting essentially of cells of a second type different from the first type.

Claims 18.–51. (Canceled)

52. (Previously presented) A three-dimensional layered structure comprising: at least one layer of a matrix; and a plurality of cell aggregates, each cell aggregate comprising a plurality of living cells; wherein the cell aggregates are embedded in the at least one layer of matrix in a non-random predetermined pattern, the cell aggregates having predetermined positions in the pattern.

53. (Previously presented) The structure of claim 52, wherein the cell aggregates are substantially uniform in size and shape.

54. (Previously presented) The structure of claim 52, wherein the cell aggregates are cylindrical.

55. (Previously presented) The structure of claim 54, wherein the cylindrical cell aggregates are from about 100 microns to about 600 microns in cross-sectional diameter.

56. (Previously presented) The structure of claim 52, wherein the cell aggregates are substantially spherical.

57. (Previously presented) The structure of claim 56, wherein the substantially spherical cell aggregates are between about 100 and about 600 microns in diameter.

58. (Previously presented) The structure of claim 52, wherein each cell aggregate comprises a plurality of living cells of a single cell type.

59. (Previously presented) The structure of claim 52, wherein at least one of the cell aggregates comprises a plurality of living cells of a first type and a plurality of living cells of a second type, the second type being different from the first type.

60. (Previously presented) The structure of claim 52, wherein the plurality of cell aggregates includes at least one cell aggregate consisting essentially of cells of a first type and at least one other cell aggregate consisting essentially of cells of a second type, the second type being different from the first type.

61. (Previously presented) The structure of claim 52, wherein the at least one layer of matrix is biocompatible and about 100 microns to about 600 microns thick.

62. (Previously presented) The structure of claim 52, wherein the at least one layer of matrix is biocompatible and selected from the group consisting of thermo-reversible gels, photo-sensitive gels, pH-sensitive gels, cell type specific gels, and combinations thereof.

63. (Previously presented) The structure of claim 52, wherein the at least one layer of matrix is biocompatible and comprises at least two different types of biocompatible matrices.

64. (Currently Amended) The structure of claim 52, comprising: a first layer of matrix; and a second layer of matrix deposited on the first layer; wherein the first layer and second layer of matrix are biocompatible; wherein the cell aggregates are embedded in the first layer and in the second layer in a predetermined pattern.

65. (Currently Amended) The structure of claim 64, further comprising at least one additional layer of matrix deposited on the second layer, wherein the at least one additional layer of matrix is biocompatible, wherein the cell aggregates are embedded in the first layer, the second layer, and the at least one additional layer in a predetermined pattern.

66. (Previously presented) The structure of claim 64, wherein the first layer comprises a type of biocompatible matrix that is different from the type of biocompatible matrix in the second layer.

Claims 67–84. (Canceled)

85. (Previously presented) The structure of claim 59, wherein the cells of the first type are smooth muscle cells and the cells of the second type are endothelial cells.

86. (Previously presented) The structure of claim 60, wherein the cells of the first type are smooth muscle cells and the cells of the second type are endothelial cells.

87. (Previously presented) The method of claim 12, wherein the cells of the first type are smooth muscle cells and the cells of the second type are endothelial cells.

88. (Previously presented) The method of claim 17, wherein the cells of the first type are smooth muscle cells and the cells of the second type are endothelial cells.

Examiner's Reasons for Allowance

The closest applicable art to instantly claimed invention is:

US2002/0182633 A1 published 05 December 2002 in favor of Chen et al.

Chen et al., teach a three dimensional structure wherein cells are arranged in an array, but the cell aggregates are not embedded in the matrix.

Thus, the prior art references cited *supra* does not teach “at a plurality of cell aggregates embedded in at least one layer of substrate as is the limitation in instantly presented Claims 52 and 1.

. Any comments considered necessary by applicants must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue

fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Claims 1-9, 11-17, 52-66 and 85-88 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:00 A.M. to 5:30 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at (571)-272-0925 Monday through Thursday 7:30 A.M. to 6:00 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kailash C Srivastava/
Examiner
Art Unit 1657
☎: 571-272-0923

/JON P WEBER/
Supervisory Patent Examiner, Art Unit 1657